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Preparation of 1-aryl-2,2-difluoro enol esters via dehydrosulfonylation of α-(phenylsulfonyl)difluoromethylated benzoates

Laijun Zhang, Ya Li, Jinbo Hu *

Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Feng-Lin Road, Shanghai 200032, China

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Abstract

1-Aryl-2,2-difluoro enol benzoates **4** has been prepared from α-(phenylsulfonyl)-difluoromethylated benzoates **3**, which can be readily obtained from the reactions between simple aldehydes and $PhSO_2CF_2H$ (or $TMSCF_2SO_2Ph$). 2,2-Difluoro enol esters **4** are relatively more stable compounds than 2,2-difluoro enol sily ethers, and they promise to act as interesting fluorinated building blocks for further elaborations.
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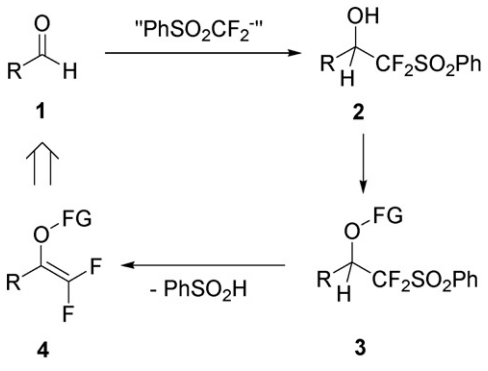
Keywords: 2,2-Difluoro enol benzoate; (Phenylsulfonyl)difluoromethyl; Dehydrosulfonylation

1. Introduction

2,2-Difluoro enol derivatives (such as 2,2-difluoro enol silyl ethers) are important fluorine-containing building blocks for the synthesis of many *gem*-difluorinated organic compounds [1–5]. Initially, 2,2-difluoro enol silyl ethers were prepared from chlorodifluoromethyl ketones [6] or from acyltrifluoromethylsilane through Brook rearrangement [7,8]. Trifluoroethanol has been widely used as an inexpensive starting material for prepation of 2,2-difluoro enol derivatives [4]. More recently, a novel C–F bond cleavage chemistry with trifluoromethyl compounds has been developed by Uneyama and co-workers, which significantly expanded both the preparation and the synthetic applications of 2,2-difluoro enol building blocks [5,9]. However, compared to the 2,2-difluoro enol silyl ethers, 2,2-difluoro enol carboxylic esters are less explored [6,8]. We envision that 2,2-difluoro enol esters can be relatively more stable than 2,2-difluoro enol silyl ethers [10], and such class of compounds can be used as interesting fluorinated building blocks for many applications.

Nucleophilic (phenylsulfonyl)difluoromethylation with $PhSO_2CF_2H$ or $TMSCF_2SO_2Ph$ reagent has increasingly become a highly useful way to synthesize structurally diverse difluoromethylated and difluoromethylenated compounds [11–13]. α-(Phenysulfonyl)difluoromethylated alcohols **2** can be readily prepared via the reactions between corresponding aldehydes and $PhSO_2CF_2H$ (or $TMSCF_2SO_2Ph$) [11b,11e,13b]. In this article, we wish to report a facile preparation of 2,2-difluoro enol esters from compounds **3** via a base-mediated dehydrosulfonylation (Scheme 1). Since compounds **3** are derived from **2** via simple benzoylation, this synthetic methodology provides a new practical approach to prepare 2,2-difluoro enol esters **4**.



Scheme 1.

* Corresponding author. Tel.: +86 21 54925174; fax: +86 21 64166128.
E-mail address: jinbohu@mail.sioc.ac.cn (J. Hu).

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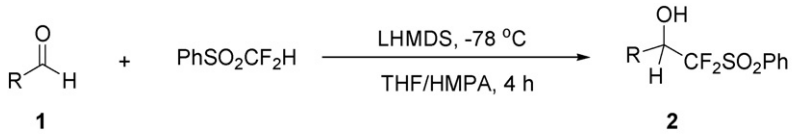


2a: R = 2-naphthyl (94%)
2b: R = Ph (81%)
2c: R = 4-methoxyphenyl (95%)
2d: R = (*E*)-PhCH=CH- (95%)
2e: R = 4-dimethylaminophenyl (95%)
2f: R = 2-methoxyphenyl (92%)
2g: R = 4-*tert*-butylphenyl (98%)
2h: R = 2-furyl (56%)
2i: R = 2-propyl (97%)

Scheme 2.

2. Results and discussion

α-(Phenylsulfonyl)difluoromethylated alcohols were prepared in high yields from aldehydes **1** and $PhSO_2CF_2H$ in the presence of lithium hexamethyldisilazide (LHMDS) according to the previous report (Scheme 2) [12e].

Initially, we observed that under the treatment of *n*-BuLi or LHMDS in THF at room temperature, compounds **2** could not undergo dehydrosulfonylation to give 2,2-difluoro enolates. However, the corresponding benzoate form (**3a**) of alcohol **2a** readily underwent dehydrosulfonylation, and the corresponding 2,2-difluoro enol benzoate **4a** could be obtained (Table 1). After a quick survey of reaction conditions, we found that adding 1.2 equiv. of LHMDS in THF at room temperature was the best conditions for the dehydrosulfonylation (Table 1, entry 3).

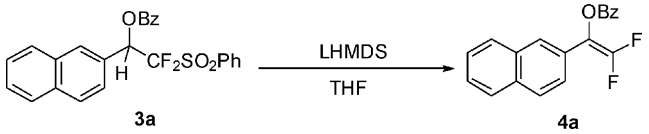
A variety of α-(phenylsulfonyl)difluoromethylated benzoates **3** were prepared from corresponding alcohols **2** in good to excellent isolated yields, following a deprotonation and benzoylation (with benzoyl chloride) sequence (Scheme 3).

By using the optimized reaction conditions (Table 1, entry 3), we then investigated the scope of the LHMDS-mediated dehydrosulfonylation reaction. The results are summarized in Table 2. For most 1-(phenylsulfonyl)difluoromethylated benzoates **3**, the dehydrosulfonylation reactions occurred smoothly to give the corresponding 1-aryl-2,2-difluoro enol benzoates **4** in moderate to good yields. The remarkable difference between *para*- and *ortho*-methoxy-substituted substrates in the reaction (entries c and e) indicates that the dehydrosulfonylation reaction is sensitive to the steric hinderance. In the case of alkyl-substituted substrate **3h** (entry h), the reaction was not successful, probably due to the difficulty in deprotonation of **3h** to generate the anionic species (Scheme 4, Eq. (2)).

α-(Phenylsulfonyl)difluoromethylated alcohol **2a** was chlorinated by phosphorus pentachloride in $CHCl_3$ at reflux temperature to give chlorinated product **5** in 81% isolated yield (Table 3, entry 3). Thionyl chloride could not chlorinate compound **2a** under similar reaction conditions, which is different from the similar chlorination of α-trifluoromethylated alcohols [14]. Mediated by LHMDS as a base in THF, compound **5** was readily dehydrosulfonylated to give 2-(1-chloro-2,2-difluorovinyl)naphthalene **6** in 54% yield (Scheme 5).

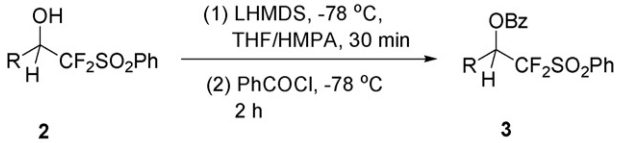
2,2-Difluoro enol benzoates **4** are stable compound at ambient temperature, which can be stored in a refrigerator for several months without any decomposition. Under KOH aqueous solution, compounds **4c** readily undergo hydrolysis to give difluoromethyl ketones **7** in 72% isolated yields (Scheme 6).

Table 1
Survey of reaction conditions for dehydrosulfonylation



Entry	LHMDS (equiv.)	Temperature (°C)	Time (min)	Yeild (%)[a]
1	1.2	−78	70	Trace
2	2	0	30	54
3	1.2	rt	60	65

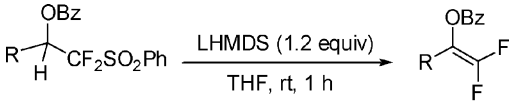
[a] Isolated yeild.



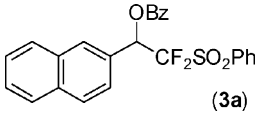
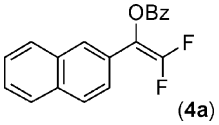
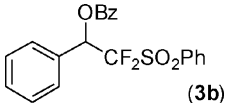
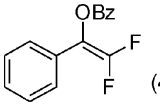
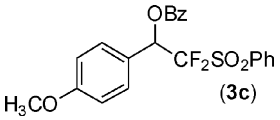
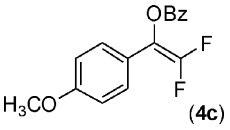
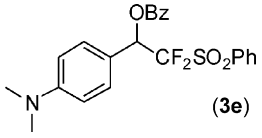
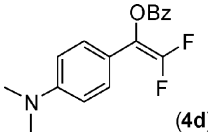
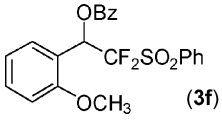
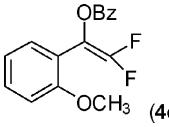
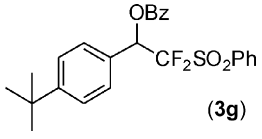
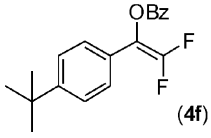
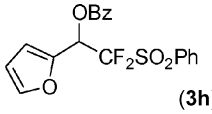
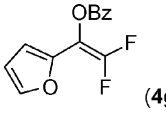
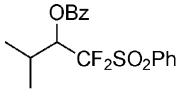
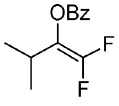
3a: R = 2-naphthyl (89%)
3b: R = Ph (92%)
3c: R = 4-methoxyphenyl (82%)
3d: R = (*E*)-PhCH=CH- (77%)
3e: R = 4-dimethylaminophenyl (90%)
3f: R = 2-methoxyphenyl (98%)
3g: R = 4-*tert*-butylphenyl (90%)
3h: R = 2-furyl (95%)
3i: R = 2-propyl (74%)

Scheme 3.

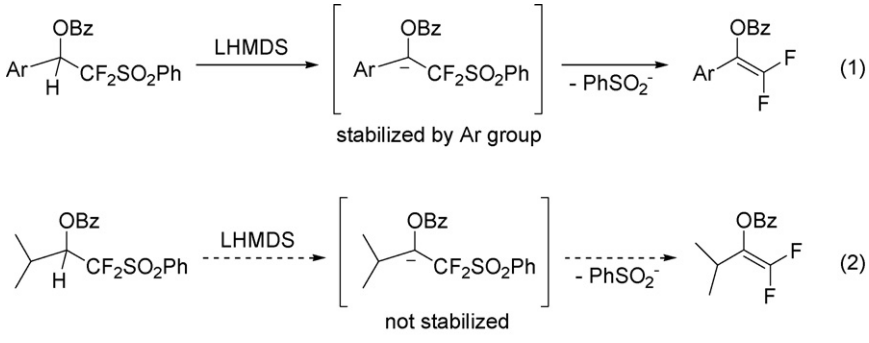
Table 2
Dehydrosulfonylation of (phenylsulfonyl)difluoromethylated benzoates **3**



3 **4**

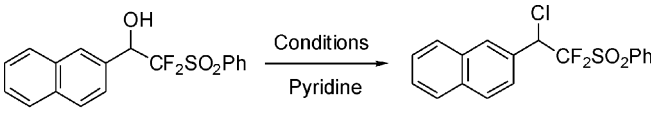
Entry	Substrate 3	Product 4	Yield (%)[a]
a	 (**3a**)	 (**4a**)	65
b	 (**3b**)	 (**4b**)	54
c	 (**3c**)	 (**4c**)	74
d	 (**3e**)	 (**4d**)	68
e	 (**3f**)	 (**4e**)	25
f	 (**3g**)	 (**4f**)	73
g	 (**3h**)	 (**4g**)	57
h	 (**3i**)	 (**4h**)	0

[a] Isolated yield.



Scheme 4.

Table 3
Chlorination of a-(phenylsulfonyl)difluoromethylated alcohol **2a**



2a **5**

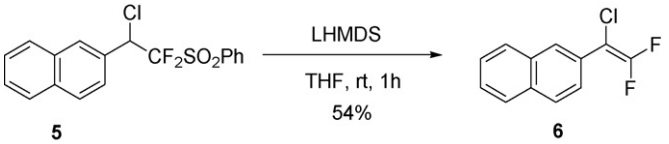
Entry	Chlorination reagent	Solvent	Temperature (°C)	Time (h)	Yeild (%)[a]
1	$SOCl_2$	Toluene	0~5	1	0
			70	2	
2	$SOCl_2$	THF	0~5	1	0
			66	2	
3	PCl_5	$CHCl_3$	60	3	81

[a]Isolated yield.

In conclusion, 1-aryl-2,2,-difluoro enol benzoates **4** has been prepared from α-(phenylsulfonyl)difluoromethylated benzoates **3**, which can be readily obtained from the reactions between simple aldehydes and $PhSO_2CF_2H$ (or $TMSCF_2SO_2Ph$). 2,2-Difluoro enol esters **4** are relatively more stable compounds than 2,2-difluoro enol sily ethers, and they promise to act as interesting fluorinated building blocks for further elaborations.

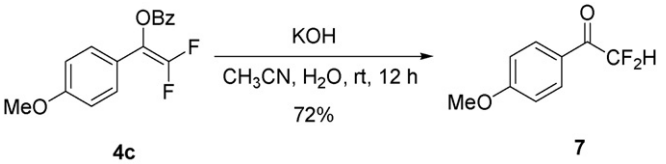
3. Experimental

Unless otherwise mentioned, solvents and reagents were purchased from commercial sources and used as received. THF was freshly distilled over sodium. Difluoromethyl phenyl sulfone was prepared using known procedures [11–13]. ^{1}H NMR spectra were recorded on Bruker 300 or Mercury 300 spectrometers with Me_4Si as internal standard. ^{19}F NMR spectra were recorded on Bruker 300 or Mercury 300 spectrometers with $CFCl_3$ as external standard. ^{13}C NMR spectra were recorded on Avance 500 or DPX-400 spectrometers. Mass spectra were obtained on a HP5989A spectrometer. High-resolution mass data were recorded on a high-resolution mass spectrometer in the EI or MALDI mode. Compounds **2** were prepared from aldehydes and $PhSO_2CF_2H$ according to previous report [12e].



5 **6**

Scheme 5.



4c **7**

Scheme 6.

3.1. Typical procedure for preparation of compounds *3*

Under N_2 atmosphere, into a 25-mL Schlenk flask containing **2b** (3.0 mmol, 0.894 g), HMPA (1.5 mL) in THF (15 mL) at −78 °C, was added dropwise a THF solution (3.40 mL) of $(TMS)_2NLi$ (LHMDS, 1.06 M, 3.60 mmol). The reaction mixture was stirred at this temperature for 30 min, followed by adding BzCl (4.5 mol, 0.632 g) and stirred for another 2 h at this temperature. The reaction mixture was quenched with saturated NH_4Cl aqueous solution, and extracted with ether (3× 25 mL). The combined organic phase was dried over $MgSO_4$. After the removal of solvents under vacuum, the crude product was purified by silica gel column chromatography to give product **3b** as a white solid (1.110 g), yield: 92%.

3.1.1. 2,2-Difluoro-1-(naphthalen-2-yl)-2-(phenylsulfonyl)ethyl benzoate (*3a*)

White solid; mp: 73–75 °C. IR (film): 3059, 1747, 1598, 1585, 1491, 1452, 1247, 1119 cm^{-1}. ^{1}H NMR: δ 8.13 (d, J = 7.6 Hz, 2H), 8.00 (t, J = 7.6 Hz, 3H), 7.83 (t, J = 8.8 Hz, 3H), 7.70–7.59 (m, 3H), 7.57–7.45 (m, 6H), 6.90 (dd, J = 19.6, 5.3 Hz, 1H). ^{19}F NMR: δ −104.14 (d, J = 243.1 Hz, 1F), −113.40 (dd, J = 242.2, 19.7 Hz, 1F). ^{13}C NMR: δ 164.085, 135.304, 133.900, 133.731, 133.450, 132.845, 130.566, 130.231, 129.280, 128.808, 128.602, 128.561, 128.530, 128.328, 127.707, 127.056, 126.563, 124.985, 120.136 (dd, J = 297.1, 284.2 Hz), 71.841 (dd, J = 30.5, 19.6 Hz), 60.347. MS (MALDI, *m/z*, %): 475.1 (M^+ + Na), 358.3 (100.00). HRMS (MALDI): calcd. for $C_{25}H_{18}F_2O_4SNa$ (M^+ + Na): 475.0786; Found: 475.0792.

3.1.2. 2,2-Difluoro-1-phenyl-2-(phenylsulfonyl)ethyl benzoate (*3b*)

White solid; mp: 106–108 °C. IR (film): 3068, 2965, 1736, 1601, 1584, 1497, 1267, 1120 cm^{-1}. ^{1}H NMR: δ 8.10 (d, J = 7.2 Hz, 2H), 7.98 (d, J = 8.1 Hz, 2H), 7.70 (t, J = 8.0 Hz, 1H), 7.61–7.53 (m, J = 8.1 Hz, 5H), 7.47 (t, J = 7.5 Hz, 2H), 7.40–7.38 (q, 3H), 6.74 (dd, J = 19.8, 5.1 Hz, 1H), ^{19}F NMR: δ −103.95 (dd, J = 243.1, 3.95 Hz, 1F), −113.27 (dd, J = 243.1, 20.6 Hz, 1F). ^{13}C NMR: δ 164.024, 135.323, 133.715, 133.477, 131.265, 130.584, 130.213, 129.931, 129.309, 128.795, 128.641, 128.520, 128.489, 119.970 (dd, J = 296.9, 283.6 Hz), 71.593 (dd, J = 30.3, 19.4 Hz). MS (EI, *m/z*, %): 261 (M^+ − SO_2Ph, 3.63), 105 (100.00). EA: calcd. for $C_{21}H_{16}F_2O_4S$: C, 62.68; H, 4.01; Found: C, 62.67; H, 4.20.

3.1.3. 2,2-Difluoro-1-(4-methoxyphenyl)-2-(phenylsulfonyl)ethyl benzoate (*3c*)

White solid; mp: 81–83 °C. IR (film): 3068, 2841, 1732, 1614, 1585, 1517, 1260, 1136 cm^{-1}. ^{1}H NMR: δ 8.08 (d, J = 7.2 Hz, 2H), 7.97 (d, J = 7.9 Hz, 2H), 7.69 (t, J = 7.4 Hz,

1H), 7.57 (m, J = 7.9 Hz, 3H), 7.45 (t, J = 8.5 Hz, 4H), 6.89 (d, J = 8.5 Hz, 2H), 6.69 (dd, J = 19.2, 5.7 Hz, 1H), 3.79 (s, 3H). ^{19}F NMR: δ −104.73 (dd, J = 240.5, 6.2 Hz, 1F), −113.53 (dd, J = 241.1, 17.2 Hz, 1F). ^{13}C NMR: δ 164.060, 160.829, 135.257, 133.628, 133.550, 130.541, 130.155, 129.970, 129.269, 128.898, 128.476, 123.192, 120.072 (dd, J = 296.6, 283.7 Hz), 114.112, 71.310 (dd, J = 30.0, 19.4 Hz), 55.253. MS (EI, *m/z*, %): 291 (M^+ − SO_2Ph, 2.49), 105 (100.00). EA: calcd. for $C_{22}H_{18}F_2O_5S$: C, 61.10; H, 4.20; Found: C, 61.09; H, 4.19.

3.1.4. (E)-1,1-Difluoro-4-phenyl-1-(phenylsulfonyl)but-3-en-2-yl benzoate (**3d**)

IR (film): 3064, 1761, 1601, 1496, 1259, 1063, 697 cm^{-1}. ^{1}H NMR: δ 8.09 (d, J = 8.4 Hz, 2H), 8.00 (d, J = 7.8 Hz, 2H), 7.71 (t, J = 7.7 Hz, 1H), 7.58 (q, J = 8.3 Hz, 3H), 7.44 (q, J = 7.1 Hz, 4H), 7.32 (m, 3H), 6.97 (d, J = 15.5 Hz, 1H), 6.44 (m, J = 7.7 Hz, 1H), 6.28 (q, J = 8.3 Hz, 1H). ^{19}F NMR: δ −106.05 (dd, J = 241.1, 8.46, Hz, 1F), −111.07 (dd, J = 241.1, 14.4 Hz, 1F). ^{13}C NMR: δ 164.299, 139.154, 135.388, 135.153, 133.658, 133.424, 130.647, 130.167, 129.334, 128.978, 128.886, 128.658, 128.491, 127.139, 117.358, 120.087 (dd, J = 293.6, 286.5 Hz), 71.399 (dd, J = 27.9, 21.6 Hz). MS (MALDI, *m/z*, %): 451.1 (M^+ + Na), 451.1 (100.00). HRMS (MALDI): calcd. for $C_{23}H_{18}F_2O_4SNa$ (M^+ + Na): 451.0786; Found: 451.0795.

3.1.5. 1-(4-(Dimethylamino)phenyl)-2,2-difluoro-2-(phenylsulfonyl)ethyl benzoate (**3e**)

White solid; mp: 115–117 °C. IR (film): 3059, 2962, 1731, 1612, 1583, 1451, 1263, 1119 cm^{-1}. ^{1}H NMR: δ 8.06 (d, J = 7.3 Hz, 2H), 7.96 (d, J = 7.8 Hz, 2H), 7.67 (t, J = 7.3 Hz, 1H), 7.60–7.50 (m, J = 7.7 Hz, 3H), 7.46–7.37 (q, J = 7.8 Hz, 4H), 6.69–6.60 (m, 3H), 2.94 (s, 6H). ^{19}F NMR: δ −104.19 (dd, J = 242.2, 7.3 Hz, 1F), −113.02 (dd, J = 241.4, 19.7 Hz, 1F). ^{13}C NMR: δ 164.128, 151.386, 135.107, 133.763, 133.441, 130.491, 130.112, 129.667, 129.202, 128.391, 120.332 (dd, J = 296.2, 283.2 Hz), 118.004, 111.850, 71.669 (dd, J = 29.9, 19.2 Hz), 40.141. MS (EI, *m/z*, %): 446 (M^+ + 1, 2.94), 105 (100.00). EA: calcd. for $C_{23}H_{21}F_2NO_4S$: C, 62.01; H, 4.75; N, 3.14; Found: C, 61.90; H, 4.91; N, 2.87.

3.1.6. 2,2-Difluoro-1-(2-methoxyphenyl)-2-(phenylsulfonyl)ethyl benzoate (**3f**)

White solid; mp: 93–95 °C. IR (film): 3071, 2983, 1730, 1601, 1589, 1494, 1341, 1247 cm^{-1}. ^{1}H NMR: δ 8.08 (d, J = 7.1 Hz, 2H), 8.01 (d, J = 7.7 Hz, 2H), 7.68 (t, J = 7.5 Hz, 1H), 7.62–7.52 (m, J = 7.5 Hz, 3H), 7.46–7.37 (q, J = 7.5 Hz, 3H), 7.37–7.27 (m, 2H), 6.93 (t, J = 7.5 Hz, 2H). 3.88 (s, 3H). ^{19}F NMR: δ −104.74 (dd, J = 244.8, 3.4 Hz, 1F), −113.98 (dd, J = 241.7, 20.3 Hz, 1F). ^{13}C NMR: δ 163.918, 157.647, 135.154, 133.732, 133.551, 130.985, 130.616, 130.174, 129.225, 129.011, 128.697, 128.466, 120.704, 120.295 (t, J = 284.4 Hz), 120.156, 111.041, 65.339 (dd, J = 32.0, 18.9 Hz), 55.959. MS (MALDI, *m/z*, %): 455.1 (M^+ + Na), 455.1 (100.00). HRMS (MALDI): calcd. for $C_{22}H_{18}F_2O_5SNa$ (M^+ + Na): 455.0735; Found: 455.0742.

3.1.7. 1-(4-tert-Butylphenyl)-2,2-difluoro-2-(phenylsulfonyl)ethyl benzoate (**3g**)

White solid; mp: 100–102 °C. IR (film): 3064, 2964, 1735, 1601, 1585, 1517, 1265, 1126 cm^{-1}. ^{1}H NMR: δ 8.08 (d, J = 7.4 Hz, 2H), 7.97 (d, J = 7.4 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.62–7.50 (m, J = 8.3 Hz, 3H), 7.48–7.43 (m, 4H), 7.38 (d, J = 8.4 Hz, 2H), 6.72 (dd, J = 20.2, 5.4 Hz, 1H). ^{19}F NMR: δ −103.69 (dd, J = 243.1, 5.1 Hz, 1F), −113.40 (dd, J = 243.1, 18.3 Hz, 1F). ^{13}C NMR: δ 164.038, 153.013, 135.227, 133.625, 133.572, 130.533, 130.174, 129.244, 128.883, 128.467, 128.222, 128.175, 125.593, 120.057 (dd, J = 296.7, 283.3 Hz), 71.409 (dd, J = 30.7, 19.2 Hz), 34.673, 31.169. MS (EI, *m/z*, %): 317 (M^+ − SO_2Ph, 1.49), 105 (100.00). EA: calcd. for $C_{25}H_{24}F_2O_4S$: C, 65.49; H, 5.28; Found: C, 65.32; H, 5.60.

3.1.8. 2,2-Difluoro-1-(furan-2-yl)-2-(phenylsulfonyl)ethyl benzoate (**3h**)

White solid; mp: 91–93 °C. IR (film): 3066, 1739, 1600, 1585, 1502, 1452, 1349, 1249 cm^{-1}. ^{1}H NMR: δ 8.06 (d, J = 8.8 Hz, 2H), 7.98 (d, J = 8.8 Hz, 2H), 7.68 (t, J = 7.6 Hz, 1H), 7.58 (q, J = 7.6 Hz, 3H), 7.45 (t, J = 7.6 Hz, 3H), 6.90 (dd, J = 17.0, 7.6 Hz, 1H). 6.68 (d, J = 3.8 Hz,1H), 6.41 (m, 1H). ^{19}F NMR: δ −105.70 (dd, J = 240.3, 6.7 Hz, 1F), −111.14 (dd, J = 240.8, 16.6 Hz, 1F). ^{13}C NMR: δ 164.061, 144.401, 135.451, 133.795, 133.166, 130.651, 130.271, 129.364, 128.500, 119.442 (t, J = 296.9 Hz), 113.019, 110.834, 65.172 (dd, J = 28.8, 20.6 Hz). MS (EI, *m/z*, %): 251 (M^+ − SO_2Ph, 1.17), 105 (100.00). EA: calcd. for $C_{19}H_{14}F_2O_5S$: C, 58.16; H, 3.60; Found: C, 58.11; H, 3.55.

3.1.9. 1,1-Difluoro-3-methyl-1-(phenylsulfonyl)butan-2-yl benzoate (**3i**)

White solid; mp: 78–80 °C. IR (film): 3069, 2970, 1741, 1602, 1582, 1492, 1340, 1259 cm^{-1}. ^{1}H NMR: δ 8.09 (d, J = 7.2 Hz, 2H), 7.97 (d, J = 7.5 Hz, 2H), 7.70 (t, J = 7.2 Hz, 1H), 7.63–7.53 (m, 3H), 7.46 (t, J = 8.0 Hz, 2H), 5.93 (ddd, J = 18.1, 8.4, 4.2 Hz, 1H), 2.53 (m, 1H), 1.09 (t, J = 7.2 Hz, 6H). ^{19}F NMR: δ −105.38 (dd, J = 241.4, 7.9 Hz, 1F), −108.70 (dd, J = 241.7, 17.5 Hz, 1F). ^{13}C NMR: δ 164.932, 135.306, 133.530, 133.143, 130.690, 130.145, 129.254, 128.961, 128.467, 121.097 (t, J = 294.8 Hz), 71.991 (dd, J = 25.7, 19 Hz), 28.850, 19.784, 16.871. MS (MALDI, *m/z*, %): 391.1 (M^+ + Na), 391.1 (100.00). HRMS (MALDI): calcd. for $C_{18}H_{18}F_2O_4SNa$ (M^+ + Na): 391.0786; Found: 391.0796.

3.2. Typical procedure for preparation of compounds **4**

Under N_2 atmosphere, into a 25 mL Schlenk flask containing **3b** (2.5 mmol, 1.005 g) in 10 mL of THF at room temperature, was added dropwise a THF solution (2.83 mL) of $(TMS)_2NLi$ (LHMDS, 1.06 M, 3.0 mmol). The reaction mixture was stirred for 1 h and quenched with saturated NH_4Cl aqueous solution, and extracted with ether (3× 25 mL). The combined organic phase was dried over $MgSO_4$. After the removal of solvents under vacuum, the crude product was purified by silica gel

column chromatography to give product **4b** as a white solid (0.353 g), yield: 54%.

3.2.1. 2,2-Difluoro-1-(naphthalene-2-yl)vinyl benzoate (*4a*)

IR (film): 3065, 1733, 1602, 1585, 1511, 1450, 1350, 1262 cm^{-1}. ^1H NMR: δ 8.17 (d, J = 7.8 Hz, 2H), 7.84–7.72 (m, 4H), 7.62 (t, J = 7.9 Hz, 1H), 7.55–7.40 (m, 5H). ^{19}F NMR: δ −91.99 (d, J = 46.8 Hz, 1F), −102.98 (d, J = 48.2 Hz, 1F). ^{13}C NMR: δ 163.883, 154.567 (t, J = 289.7 Hz), 134.078, 133.034, 132.974, 130.410, 128.773, 128.533, 128.434, 128.286, 127.648, 126.746, 126.609, 125.062 (t, J = 5.2 Hz), 122.840, 122.794, 122.772. MS (EI, *m/z*, %): 310 (M^+, 5.95), 105 (100.00). EA: calcd. for $C_{19}H_{12}F_2O_2$: C,73.54; H, 3.90; Found: C,73.29; H, 4.04.

3.2.2. 2,2-Difluoro-1-phenylvinyl benzoate (*4b*)

White solid; mp: 18–20 °C. IR (film): 3065, 1749, 1601, 1585, 1500, 1452, 1259, 1135 cm^{-1}. ^1H NMR: δ 8.20 (d, J = 6.9 Hz, 2H), 7.65 (t, J = 7.3 Hz, 1H), 7.54–7.46 (q, J = 8.2 Hz, 4H), 7.41–7.30 (m, J = 6.9 Hz, 3H). ^{19}F NMR: δ −92.55 (d, J = 47.4 Hz, 1F), −103.18 (d, J = 47.6 Hz, 1F). ^{13}C NMR: δ 163.817, 154.361 (t, J = 289.0 Hz), 134.036, 130.356, 128.881, 128.830, 128.733, 128.680, 128.466, 128.407, 125.520 (dd. J = 6.3, 4.0 Hz). MS (EI, *m/z*, %): 260 (M^+, 0.99), 105 (100.00). HRMS (EI): calcd. for $C_{15}H_{10}F_2O_2$: 260.0649; Found: 260.0639.

3.2.3. 2,2-Difluoro-1-(4-methoxyphenyl)vinyl benzoate (*4c*)

White solid; mp: 44–45 °C. IR (film): 3004, 2844, 1742, 1610, 1574, 1516, 1260, 1114 cm^{-1}. ^1H NMR: δ 8.19 (d, J = 8.0 Hz, 2H), 7.66 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 8.0 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H). ^{19}F NMR: δ −94.28 (d, J = 52.7 Hz, 1F), −104.89 (d, J = 52.5 Hz, 1F). ^{13}C NMR: δ 163.874, 159.674, 153.993 (dd. J = 288.7, 286.8 Hz), 133.966, 130.321, 128.701, 128.516, 127.144 (dd. J = 6.1, 4.0 Hz), 121.674, 121.611, 114.196, 55.286. MS (EI, *m/z*, %): 290 (M^+, 2.58), 105 (100.00). EA: calcd. for $C_{16}H_{12}F_2O_3$: C, 66.21; H, 4.17; Found: C, 65.95; H, 4.50.

3.2.4. 1-(4-(Dimethylamino)phenyl)-2,2-difluorovinyl benzoate (*4d*)

White solid; mp: 108–109 °C. IR (film): 3068, 2897, 1744, 1618, 1584, 1529, 1280, 1115 cm^{-1}. ^1H NMR: δ 8.18 (d, J = 8.4 Hz, 2H), 7.65 (t, J = 7.8 Hz, 1H), 7.51 (t, J = 7.9 Hz, 2H), 7.33 (d, J = 9.0 Hz, 2H), 6.69 (d, J = 9.0 Hz, 2H), 2.96 (s, 6H). ^{19}F NMR: δ −95.92 (d, J = 56.4 Hz, 1F), −106.48 (d, J = 57.2 Hz, 1F). ^{13}C NMR: δ 163.954, 153.780 (dd, J = 287.5, 285.4 Hz), 150.315, 133.797, 130.298, 128.638, 126.821, 126.786, 126.768, 126.727, 112.127, 40.228. MS (EI, *m/z*, %): 303 (M^+, 13.78), 105 (100.00). EA: calcd. for $C_{17}H_{15}F_2NO_2$: C, 67.32; H, 4.98; N, 4.62; Found: C, 67.21; H, 5.20; N, 4.41.

3.2.5. 2,2-Difluoro-1-(2-methoxyphenyl)vinyl benzoate (*4e*)

IR (film): 3066, 2941,1748, 1602, 1583, 0496, 1249, 1126 cm^{-1}. ^1H NMR: δ 8.12 (d, J = 7.8 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 7.49–7.42 (q, J = 7.4 Hz, 3H), 7.36 (t, J = 8.2 Hz, 1H), 7.00–6.91 (q, J = 8.5 Hz, 2H), 3.82 (s, 3H). ^{19}F NMR: δ −94.19 (d, J = 48.2 Hz, 1F), −103.62 (d, J = 48.2 Hz, 1F). ^{13}C NMR: δ 163.871, 157.550, 154.00 (dd, J = 289.4, 283.1 Hz), 133.603, 131.007, 130.806, 130.221, 128.966, 128.510, 120. 487, 111.377, 55.713. MS (EI, *m/z*, %): 290 (M^+, 2.33), 105 (100.00). HRMS (EI): calcd. for $C_{16}H_{12}F_2O_3$: 290.0755; Found: 290.0764.

3.2.6. 1-(4-tert-Butylphenyl)-2,2-difluorovinyl benzoate (*4f*)

White solid; mp: 40–41 °C. IR (film): 2972, 1751, 1601, 1585, 1492, 1278, 1138 cm^{-1}. ^1H NMR: δ 8.19 (d, J = 7.5 Hz, 2H), 7.66 (t, J = 7.1 Hz, 1H), 7.52 (t, J = 7.5 Hz, 2H), 7.40 (s, 4H), 1.30 (s, 9H). ^{19}F NMR: δ −92.95 (d, J = 49.4 Hz, 1F), −103.47 (d, J = 49.4 Hz, 1F). ^{13}C NMR: δ 163.867, 157.174, 154.283, 151.621, 133.970, 130.343, 128.709, 128.509, 126.405, 125.649, 125.279 (dd, J = 6.1, 3.3 Hz), 34.641, 31.162. MS (EI, *m/z*, %): 316 (M^+, 2.36), 105 (100.00). HRMS (EI): calcd. for $C_{19}H_{18}F_2O_2$: 316.1275; Found: 316.1286.

3.2.7. 2,2-Difluoro-1-(furan-2-yl)vinyl benzoate (*4g*)

IR (film): 3068, 1751, 1602, 1585, 1494, 1454, 1271 cm^{-1}. ^1H NMR: δ 8.18 (d, J = 7.6 Hz, 2H), 7.66 (t, J = 6.8 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H), 7.44 (s, 1H), 6.45 (s, 2H). ^{19}F NMR: δ −94.44 (d, J = 43.7 Hz, 1F), −100.39 (d, J = 43.7 Hz, 1F). ^3C NMR: δ 171.743, 149.399, 134.885, 133.827, 130.505, 130.198, 130.039, 128.840, 128.594, 128.481, 123.192 (t, J = 4.1 Hz), 112.965, 110.865. MS (EI, *m/z*, %): 250 (M^+, 1.84), 105 (100.00). HRMS (EI): calcd. for $C_{13}H_8F_2O_3$: 250.0442; Found: 250.0448.

3.3. Preparation of compound *5*

Under N_2 atmosphere, into a 50-mL Schlenk flask containing **2a** (2.0 mmol, 0.696 g), $CHCl_3$ (30 mL), PCl_5 (6.0 mmol, 1.252 g) at room temperature, was added dropwise pyridine (12.0 mmol, 0.936 g). The reaction mixture was heated at reflux temperature for 3 h. After quenched with ice-water, the reaction mixture was extracted with $CHCl_3$ (3× 30 mL), and the combined organic phase was dried over anhydrous $MgSO_4$. The volatile solvents were removed under vacuum, and the crude product was purified by silica gel column chromatography to give product **5** as a white solid (0.592 g), yield: 81%.

3.3.1. 2-(1-Chloro-2,2-difluoro-2-(phenylsulfonyl)ethyl)naphthalene (*5*)

White solid; mp: 136–138 °C. IR (film): 3064, 1581, 1509, 1449, 1340, 1157, 1108 cm^{-1}. ^1H NMR: δ 7.98 (s, 1H), 7.83 (d, J = 8.2 Hz, 5H), 7.68–7.44 (m, 6H), 5.78 (dd, J = 15.7, 10.4 Hz, 1H). ^{19}F NMR: δ −102.22 (dd, J = 230.7, 10.2 Hz, 1F), −105.90 (dd, J = 232.1, 16.1 Hz, 1F). ^{13}C NMR: δ 135.310, 133.899, 133.256, 132.694, 130.565, 129.864, 129.379,

129.127, 128.776, 128.416, 127.724, 127.422, 126.757, 125.607, 120.179 (t, J = 292.9 Hz), 57.830 (t, J = 21.9 Hz). MS (EI, *m/z*, %): 366 (M^+, 3.28), 190 (100.00). HRMS (EI): calcd. for $C_{18}H_{13}F_2O_2ClS$: 366.0293; Found: 366.0306.

3.4. Preparation of compound **6**

Under N_2 atmosphere, into a 25-mL Schlenk flask containing **5** (1.5 mmol, 0.549 g) in 15 mL of THF at room temperature, was added dropwise a THF solution (1.70 mL) of $(TMS)_2NLi$ (LHMDS, 1.06 M, 1.8 mmol). The reaction mixture was stirred for 1 h and quenched with saturated NH_4Cl aqueous solution, and extracted with ether (3× 25 mL). The combined organic phase was dried over $MgSO_4$. After the removal of solvents under vacuum, the crude product was purified by silica gel column chromatography to give product **6** as a white solid (0.182 g), yield: 54%.

3.4.1. 2-(1-Chloro-2,2-difluorovinyl)naphthalene (**6**)

White solid; mp: 42–44 °C. IR (film): 3061, 2925, 1718, 1627, 1296, 1274, 1193, 1006 cm^{-1}. ^1H NMR: δ 8.00 (s, 1H), 7.84 (m, 3H), 7.61 (d, J = 8.7 Hz, 1H), 7.55–7.49 (m, J = 3.1 Hz, 2H). ^{19}F NMR: δ −82.74 (d, J = 31.3 Hz, 1F), −88.52 (d, J = 32.7 Hz, 1F). ^{13}C NMR: δ 157.079, 154.173, 151.290, 133.070, 132.870, 128.303, 127.641, 127.045, 126.736, 124.824, 124.669 (dd. J = 5.2, 2.2 Hz), 121.026. MS (EI, *m/z*, %): 224 (M^+, 97.95), 44 (100.00). HRMS (EI): calcd. for $C_{12}H_7ClF_2$: 224.0204; Found: 224.0196.

3.5. Typical procedure for the hydrolysis of compound **4**

Into a 10-mL Schlenk flask containing **4c** (0.2 mmol, 0.058 g), THF (2 mL), H_2O (2 mL) at room temperature, was added KOH (0.3 mmol, 0.017 g). The reaction mixture was stirred for 12 h, and extracted with ether (3× 25 mL). The combined organic phase was dried over $MgSO_4$. After the removal of solvents under vacuum, the crude product was purified by silica gel column chromatography to give product **7** as a colorless liquid (0.027 g), yield: 72%.

3.5.1. 2,2-Difluoro-1-(4-methoxyphenyl)ethanone (**7**)

^1H NMR: δ 7.99 (d, J = 8.7 Hz, 2H), 6.92 (d, J = 8.7 Hz, 2H), 6.19 (t, J = 53.7 Hz, 1H), 3.83 (s, 3H). ^{19}F NMR: δ −121.8 (d, J = 51.8 Hz). The characterization data was consistent with the previous report [15].

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